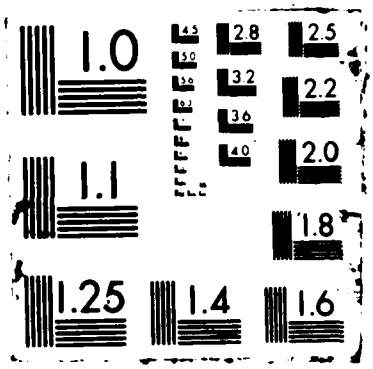
AD-A184 838 STUDIES ON SYNTHESES OF AMINE-CARBOXYBORANES (BORON ANALOGUES OF AMINO AC..(U) DUKE UNIV DURHAM NC B F SPIELVOGEL ET AL. 17 AUG 87 ARO-20852.10-CH 1/1

UNCLASSIFIED DAAG29-79-D-1001 F/G 7/3 NL


1.0
1.1
1.25
1.4
1.6
2.8
2.5
3.2
2.2
3.6
2.0
4.0
1.8

DTIC FILE COPY

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

MASTER COPY - FOR REPRODUCTION PURPOSES

AD-A184 838

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

REPORT NUMBER	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
ARO 20852.10-CH	N/A	N/A

(2)

TITLE (and Subtitle)

Studies on Syntheses of Amine-Carboxyboranes (Boron Analogues of Amino Acids) and Derivatives

5. TYPE OF REPORT & PERIOD COVERED: 1 Sep 83 - 31 May 87 Final

6. PERFORMING ORG. REPORT NUMBER

AUTHOR(s)

Bernard F. Spielvogel and Andrew T. McPhail

8. CONTRACT OR GRANT NUMBER(s): DAAG29-79-D-1001

PERFORMING ORGANIZATION NAME AND ADDRESS

Duke University
Durham, North Carolina 27706

10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS

CONTROLLING OFFICE NAME AND ADDRESS

U. S. Army Research Office
Post Office Box 12211
Research Triangle Park, NC 27709

12. REPORT DATE: August 17, 1987

13. NUMBER OF PAGES: 5

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)

15. SECURITY CLASS. (of this report): Unclassified

15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

DTIC ELECTE SEP 17 1987 D

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

NA

18. SUPPLEMENTARY NOTES

The view, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other documentation.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Boron, amino acids, acetylcholine, antitumor, hypolipidemic

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The principal goal of this research has been the synthesis and characterization of boron analogues of important biologically active molecules such as the amino acids. During this period of research syntheses were developed for esters and amides of a variety of simple boron analogues of amino acids. Also, routes to boron analogues of choline, acetylcholine and substituted acetylcholines were developed. Collaborative studies on the biological activity of many of these compounds were carried out by Professor Iris H. Hall at the University of North Carolina (cont.)

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

Studies on Syntheses of Amine-Carboxyboranes

(Boron Analogues of Amino Acids) and Derivatives

Final Report

Bernard F. Spielvogel and Andrew T. McPhail

August 17, 1987

Duke University
Durham, N.C. 27706

Contract No. DAAG29-79-D-1001
ARO Proposal No. 20852-CH

Accesion For
NTIS CRA&I
DTIC TAB
Unannounced
Justification
By
Distribution/
Availability Codes
Dist | Avail and/or Special
A-1

QUALITY INSPECTED 2

87 9 16 140

The principal goal of this research has been the synthesis and characterization of boron analogues of impo-tant biologically active molecules such as the amino acids. During this period of research syntheses were developed for esters and amides of a variety of simple boron analogues of amino acids. Also, routes to boron analogues of choline, acetylcholine and substituted acetylcholines were developed. Collaborative studies on the bilogical activity of many of these compounds were carried out by Professor Iris H. Hall at the University of North Carolina. Significant antitumor and hypolipidemic activity have been found in animal model studies.

PUBLICATIONS

1. B. F. Spielvogel, A. T. McPhail, J. A. Knight, G. C. Moreland, C. L. Gatchell and K. W. Morse, "Predictive Schemes for the Reactivity of Borane Carbonyl and the Stability of Carbonyltrihydroborate Anions, $BH_3C(0)X^-$", Polyhedron, 2, 1345 (1983).

2. B. F. Spielvogel, A. T. McPhail, I. H. Hall, R. G. Fairchild and P. L. Micca, "Boron Analogues of α-Amino Acids" Proceedings of the First International Symposium on Neutron Capture Therapy, DOE Report BNL 51730, October 12-14, 1983.

3. I. H. Hall, B. F. Spielvogel and A. T. McPhail, "Antineoplastic Activity of Tetrakis-(μ-)trimethylamine-boranecarboxylato)-bis(trimethylaminecarboxyborane)dicopper(II) in Ehrlich Ascites Carcinoma", J. Pharm. Sci., 73, 222 (1984).

4. B. F. Spielvogel, F. U. Ahmed, K. W. Morse and A. T. McPhail, "Boron Analogues of Amino Acids. 3. Synthesis of (Ethylcarbamoyl) borane Adducts of Me_3N, Me_2N, Me_2NH, $MeNH_2$, and NH_3", Inorg, Chem. 23, 1776 (1984).

5. B. F. Spielvogel, F. U. Ahmed, G. L. Silvey, P. Wisian-Neilson and A.T. McPhail, "Boron Analogues of Amino Acids. 4. Synthesis of Glycine and N-Methylated Glycine Ester Analogues", Inorg. Chem. 23, 4322 (1984).

6. B. F. Spielvogel, F. U. Ahmed, M. K. Das and A. T. McPhail, "Synthesis of Sodium and Tetra-n-Butylammonium dicyanodihydroborate", Inorg. Chem. 23, 3263 (1984).

7. I. H. Hall, W. Williams, C. J. Gilbert, A. T. McPhail, B. F. Spielvogel, "The Hypolipidemic Activity of Tetrakis-μ-(trimethylamine-boranecarboxylato)-bis(trimethylamine-carboxyborane)dicopper(II) in Rodents and its Effect on Lipid Metabolism", J. Pharm. Sci. 73, 973 (1984).

8. I. H. Hall, C. J. Gilbert, A. T. McPhail, K.W. Morse and B. F. Spielvogel, "The Antineoplastic Activity of a Series of Boron Analogues of Amino Acids", J. Pharm. Sci. 24 765 (1985).

9. H. Hakemi, F. U. Ahmed, W. R. Krigbaum, A. T. McPhail and B. F. Spielvogel, "Investigation of Mixtures of Cholesteryl Esters of Boron Analogues of Amino Acids with P-Azoxyanisole" Mol. Cryst.Liq. Cryst. 128, 65(1985).

10. Bernard F. Spielvogel, Fahim U. Ahmed and Andrew T. McPhail, "Boron Analogues of Amino Acids. 5. A Simple, Convenient Method for the Esterification of Amine-carboxyboranes." Synthesis. 833 (1986).

11. Bernard F. Spielvogel, Fahim U. Ahmed and Andrew T. McPhail, "A Remarkably Facile Synthesis of An Isoelectronic and Isostructural Boron Analogue of Acetylcholine." J. Amer. Chem. Soc. 108 3824 (1986).

12. B. F. Spielvogel, "Pharmacologically Active Boron Analogues of Choline 2. Efficient Synthesis of Boron Analogues of Choline, Acetylcholine, and Substituted Acetylcholines." Inorg. Chem. 25,4395 (1986).

13. B. F. Spielvogel, "Pharmacologically Active Boron Analogues of Amino Acids" Molecular Structure and Energetics. Vol 5, Advances in Boron and the Boranes, R. E. Williams, Ed. VCH Publishers, Inc. New York, N.Y. (1987) in press.

14. I. H. Hall, B. F. Spielvogel, A. Sood, F. Ahmed and S. Jafri, "Hypolipidemic Activity of Trimethyamine-Carboxyborane and Related Derivatives in Rodents" J. Pharm. Sci. 76, 359 (1987).

15. B. F. Spielvogel, F. U. Ahmed, A. T. McPhail "Boron Analogues of Amino Acids" "Inorganic Syntheses" H. R. Allcock, Ed. Vol 26, in press.

Personnel Supported

Dr. A. T. McPhail
Dr. F. U. Ahmed
G. L. Silvey (Ph.D. obtained)
Dr. A. Sood
C. Sood
S. Jafri

END

11-87

DTIC